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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/316,387	05/21/1999	ALAN SOLOMON	044137-5025	7724

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EXAMINER
TURNER, SHARON L

ART UNIT	PAPER NUMBER
1647	15

DATE MAILED: 04/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/316,387	Solomon et al.
Examiner	**Art Unit**
Sharon L. Turner, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on 2-4-02

2a) [X] This action is **FINAL.** 2b) [ ] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) 10-45 is/are pending in the applica

4a) Of the above, claim(s) 10-22, 28, and 36 is/are withdrawn from considera

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) 23-27, 29-35, and 37-45 is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [X] Claims 10-45 are subject to restriction and/or election requirem

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____.
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) [X] Notice of References Cited (PTO-892)

16) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) [ ] Interview Summary (PTO-413) Paper No(s). _____

19) [ ] Notice of Informal Patent Application (PTO-152)

20) [ ] Other:

Response to Amendment

1. The amendment filed 7-18-01 has been entered into the record and has been fully considered.

2. As a result of applicants amendment, all rejections not reiterated herein have been withdrawn by the examiner.

3. Claims 10-45 are pending.

Election/Restriction

4. Applicant's election with traverse of species monoclonal antibodies reactive with a non-light chain amyloid, identified by applicants as claims 23-36 and 39-45 in Paper No. 14 (2-4-02) is acknowledged. The traversal is on the ground(s) that the Office Action fails to provide evidence of any significant search burden with respect to the delineated species. This is not found persuasive because as set forth the species are patentably distinct as they lack a common core structure and differ in functional properties with different use, different modes of operation, different functions and different effects. Thus a search for any one of the species would not reveal all pertinent art to any other species and thus the search and examination of all species in a single application may place an undue burden upon the Examiner.

The requirement is still deemed proper and is therefore made FINAL.

5. Newly submitted claims 28 and 36 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Applicants have elected

species of monoclonal antibodies reactive with a non-light chain amyloid. Applicants have identified the elected invention as readable on claims 28 and 36. However, claims 28 and 36 are drawn to antibodies raised against immunoglobulin light chain and to monoclonal antibodies reactive with immunoglobulin light chains and thus are directed to non-elected species.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 28 and 36 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

6. Claims 10-22 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as set forth in Paper No's 7 and 10 as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 8.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 23-27, 29-31, 35, 40- 42 and 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Konig et al., WO96/25435, 22 August 1996

Konig et al., teach methods of diagnosis, screening and therapeutics for treating unique forms of amyloid peptide deposition using antibodies. Konig et al., teach administration of monoclonal antibodies which bind amyloid fibrils, see in particular claims 9-20 and pp. 6-8 for treatment of Alzheimer's disease. The antibodies specifically bind amyloid fibrils, see in particular p. 6, line 25. Thus, the reference teaches a method which comprises treating a patient having an amyloid deposition disease by administration of an immunoglobulin polypeptide which binds to an amyloid fibril. Konig further teaches that the antibody treatment is effective in a method for the prevention of aggregation of beta amyloid peptide by administration of the antibody, see in particular p. 7, lines 21-23, p. 13, lines 17-20, p.14, lines 6-11 and p. 25, lines 14-18. As the antibodies bind beta amyloid as taught by Konig they are inherently effective to remove the amyloid plaque via opsonization. The antibodies can be provided in sterile saline or a pharmaceutically acceptable carrier such as Keyhole Limpet Hemocyanin, see in particular p. 17. Thus, the mechanistic recitation of inhibiting formation and modulation of amyloid deposition are inherently achieved as preventing aggregation is taught. Further, prevention of aggregation inherently inhibits the rate of formation of amyloid deposits as claimed in claim 26. The antibodies may be labeled by biotinylation or with radioactive tags such as 35S-Met, see in particular p.22. Konig further notes at p. 5-7 suitable cross-reactive antibodies and epitopes for various modifications. Specific embodiments of monoclonals are disclosed from p. 19-23.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 23-27, 29-35, 37-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Walker et al., J. of Neuropathol. & Exp. Neurol., 53(4):377-83, July 199, Konig et al., WO96/25435, 22 August 1996, Nettleship et al., EP613007, 8-31-1994 and Immunology: a short course, Benjamini & Leskowitz Ed., Wiley-Liss, Inc., New York, NY, page 142.

Walker et al., teach in vivo administration of monoclonal antibody specific to labeling amyloid fibrils for therapeutic purposes, see in particular abstract. Walker et al., teach administration of monoclonal antibody 10D5 to living nonhuman primates. 10D5 specifically bound amyloid deposits in cerebral cortex and thus the method comprises treating a patient

having an amyloid deposition disease by administration of an immunoglobulin polypeptide which binds to an amyloid fibril, see in particular abstract. The injection was provided in sterile saline, a pharmaceutically acceptable carrier, see in particular p. 378, column 1, Injection of antibody, lines 1-2. The antibody intrinsically opsonizes upon binding, as evidenced by Benjamini et al., which teach at p. 142 that IgG immunoglobulin antibodies bind and mediate opsonization or removal via phagocytosis. Thus, the artisan would equate the mechanistic recitation of inhibiting formation, removal or modulation of amyloid deposition as being achieved.

Konig et al., teach methods of diagnosis, screening and therapeutics for treating unique forms of amyloid peptide deposition using antibodies. Konig et al., teach administration of monoclonal antibodies which bind amyloid fibrils, see in particular claims 9-20 and pp. 6-8 for treatment of Alzheimer's disease. The antibodies specifically bind amyloid fibrils, see in particular p. 6, line 25. Thus, the reference teaches a method which comprises treating a patient having an amyloid deposition disease by administration of an immunoglobulin polypeptide which binds to an amyloid fibril. Konig further teaches that the antibody treatment is effective in a method for the prevention of aggregation of beta amyloid peptide by administration of the antibody, see in particular p. 7, lines 21-23, p. 13, lines 17-20, p.14, lines 6-11 and p. 25, lines 14-18. The antibodies can be provided in sterile saline or a pharmaceutically acceptable carrier such as Keyhole Limpet Hemocyanin, see in particular p. 17. The antibody intrinsically opsonizes upon binding, as evidenced by Benjamini et al., which teach at p. 142 that IgG

immunoglobulin antibodies bind and mediate opsonization or removal via phagocytosis. Thus, the artisan would equate the mechanistic recitation of inhibiting formation, removal or modulation of amyloid deposition as being achieved. The antibodies may be labeled by biotinylation or with radioactive tags such as 35S-Met, see in particular p.22. Konig further notes at p. 5-7 suitable cross-reactive antibodies and epitopes for various modifications. Specific embodiments of monoclonals are disclosed from p. 19-23.

Nettleship et al., teach antibodies useful in the diagnosis and treatment of mammals suffering from Alzheimer's Disease, see in particular column 7, line 39- column 8, line 18. The antibodies are beta-amyloid peptides, particularly in beta-sheet conformation, but also include antibodies to alternative fragments, see in particular column 1, line 52-column 2, line 56. It is understood that the functional embodiment which characterizes the diagnostic and therapeutic relationship as disclosed in Nettleship hinges on the binding of the antibodies to the beta-amyloid peptides, see in particular reference in paragraph spanning columns 7-8 and reference to numerous assay systems suitable to detect agents which bind, column 8, lines 6-15. In addition, the compositions are pharmaceutical compositions which include formulations for parenteral administration (other than by intestinal, i.e., subcutaneous, intravenous, etc., as understood by the skilled artisan), see in particular column 8, lines 19-42. Thus, the reference appears to be enabling for the determination of appropriate doses and routes of administration suitable for such binding, inhibition of formation, removal or modulation of amyloid deposition to occur. Nettleship et al., teach the use of alternatively produced Aβ antibodies including to peptides

which have adopted a random coil or alpha-helix conformation and to antibodies which are genetically engineered, antibody fragments, chimeric antibodies, recombinantly produced antibodies, and "humanized or murinized" antibodies as generated by replacement of CDR regions, see in particular column 5, lines 42-column 6, line 20. Thus the reference teaches the variable or cross reactive antibodies of the claims. It is noted that the polyclonal sera would inherently include multiple antibodies and Ig isotypes. It is further noted that the patient population includes mammals and thus encompass humans and human antibodies, see in particular columns 6-7.

Applicants specification at pp. 14-16 also teach the routine of one of skill in the art to produce humanized and chimeric antibodies.

Neither Walker, Konig or Nettleship specifically teach the mechanistic effects of antibody administration as recited in the claims, i.e., the inhibition of formation, removing amyloid deposits or the modulation of formation of amyloid deposits. However, Konig et al., teaches that antibody administration is effective to prevent aggregation of amyloid into amyloid deposits and Walker and Nettleship teach the use of antibody administration for the treatment and prevention of Alzheimer's Disease mediated via preventing and treating amyloid deposition. However, Benjamini et al., teach as recognized in the art that antibody binding mediates opsonization and removal of the bound material in the host.

Thus, it would have been prima facie obvious to the skilled artisan to utilize either the antibodies of either Walker, Konig or Nettleship for the in vivo administration and treatment of

patients, particularly with Alzheimer's Disease. Further it would have been prima facie obvious based on the teachings of Konig and Benjamini that such treatment is effective to prevent aggregation of beta-amyloid deposition, and that such inhibition resulting from antibody binding would be effective to inhibit the formation of amyloid deposits, remove amyloid deposits and or modulate the levels of amyloid deposition in patients. One of skill in the art would have been motivated to provide such a method based on the cumulative reference teachings and the recognition in the art of opsonization based upon antibody binding to beta-amyloid. The effective amounts are provided by the antibody compositions effective for binding and routing. Further, one skilled in the art would have expected success using such a method based upon the high skill in the art of antibody technology and the combined teachings of Walker, Konig, Nettleship and Benjamini in the treatment of amyloid deposition disease with non-light chain, beta-amyloid antibody. Thus, for the aforementioned reasons, the claimed invention is rendered obvious to the skilled artisan.

Status of Claims

11. No claims are allowed.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
April 22, 2002

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Sharon L. Turner, Ph.D.
April 15, 2002

Gary L. Kunz

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